Characterization and In Vivo Testing of Mesenchymal Stem Cells Derived From Human Embryonic Stem Cells.

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Public Summary:
Human mesenchymal stem cells (MSC) from the bone marrow are excellent delivery vehicles to produce factors to promote tissue healing and disease modification. However the use of integrating viral vector techniques to augment the MSC can carry risks, since the vectors could potentially integrate into an active gene. For this reason it would be optimal to create banks of MSC from pluripotent cells, where a "safe harbor" integration site could be targeted and cells expanded clonally before creation of large numbers of MSCs. This reason motivated us to examine differentiation of human MSC from the embryonic stem cell line H9, and to characterize them in vitro and after transplantation into an immune deficient mouse model of limb ischemia. We found that they behaved in very similar ways to adult MSC. This study could be important for making banks of gene-modified MSC with "safe harbor" integration sites, for future therapeutic applications.

Scientific Abstract:
Mesenchymal stem cells (MSC) have been shown to contribute to the recovery of tissues through homing to injured areas, especially to hypoxic, apoptotic, or inflamed areas and releasing factors that hasten endogenous repair. In some cases genetic engineering of the MSC is desired, since they are excellent delivery vehicles. We have derived MSC from the hESC line H9 (H9-MSC). They expressed CD105, CD90, CD73 and CD146, and lacked expression of CD45, CD34, CD14, CD31, and HLA-DR, the hESC pluripotency markers SSEA-4 and Tra-1-81, and the hESC early differentiation marker SSEA-1. Marrow-derived MSC showed a similar phenotype. H9-MSC did not form teratoma in our initial studies, whereas the parent H9 line did so robustly. H9-MSC differentiated into bone, cartilage and adipocytes in vitro, and displayed increased migration under hypoxic conditions. Finally, using a hindlimb ischemia model, H9-MSC were shown to home to the hypoxic muscle, but not the contralateral limb, by 48 hours after IV injection. In summary, we have defined methods for differentiation of hESC into MSCs and have defined their characteristics and in vivo migratory properties.

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